BLUE-GREEN ALGAE

MEDITEXT ® - Medical Management

0.0 OVERVIEW

0.1 LIFE SUPPORT

A) This overview assumes that basic life support measures have been instituted.

0.2 CLINICAL EFFECTS

0.2.1 SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

A) HUMANS - Ingestion of concentrations high enough to cause serious toxicity is uncommon. Gastrointestinal effects following ingestion and dermatitis following contact are the most common effects.

1) Pneumonia (uncommon), sore throat, fever, vomiting, diarrhea, lassitude, rhinitis, conjunctivitis, perioral blisters, dermatitis, mild liver enzyme elevations, and electrolyte imbalance have been reported.

2) GASTROINTESTINAL EFFECTS may include the following:

a) ONSET - 3 to 5 hours (abdominal cramping, diarrhea, nausea, vomiting)

b) SEVERITY - generally mild; can be severe

c) DURATION - usually 1 to 2 days

d) Adverse effects have resulted from immersion in or consumption of contaminated water, ingestion of fish from contaminated water, and recreation on waters which have cyanobacteria. The tastes and odors of contaminated water generally limit the amounts ingested.

3) Fatal hepatic failure was reported following the use of contaminated water in a hemodialysis unit in Brazil.

B) ANIMALS - The toxins are potent neuromuscular blocking agents in animals.

1) A characteristic animal death caused by one kind of blue-green algae (Aphanizomenon) includes irregular respirations, spastic twitching, loss of coordination, violent tremors, gaping mouth, and death by respiratory failure. The onset depends on species. Death may be rapid (animals die before they leave the water) or delayed 6 to 24 hours.

2) Animals do not like to drink the contaminated water, but will if sufficiently thirsty.

C) The effects seem to be much more serious in animals than in humans. It is not known if this is due to lower ingested doses in humans or differences in the reaction of animals to the toxin as compared to humans.

0.2.3 VITAL SIGNS

0.2.4 HEENT

0.2.4.1 ACUTE EXPOSURE

A) Human effects include conjunctivitis, earache, swollen lips, and headache.

0.2.6 RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

A) Atypical pneumonia and a hay-fever like syndrome have been reported.

0.2.7 NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

A) Headache and malaise have occurred in humans. Partial paralysis and respiratory paralysis has been reported in animals and birds.

0.2.8 GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

A) Human reports include nausea, vomiting and diarrhea. Cases may appear as enteritis or amebic dysentery. Onset is 3 to 5 hours post ingestions, with recovery in 1 to 2 days.

0.2.9 HEPATIC

0.2.9.1 ACUTE EXPOSURE

A) Elevated liver enzymes were documented in residents who drank from a contaminated reservoir.

B) Hepatic failure occurred in dialysis patients from microcystin contaminated water.

0.2.10 GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

A) Glycosuria, proteinuria, and occasionally hematuria have been reported.

0.2.15 MUSCULOSKELETAL

0.2.15.1 ACUTE EXPOSURE

A) Humans have reported muscle weakness and pain in the limbs and joints.

0.2.17 METABOLISM

0.2.17.1 ACUTE EXPOSURE

A) Anatoxin A is known to have anticholinesterase activity, based on effects in animals.

0.2.22 GENOTOXICITY

A) M. aeruginosa extracts fed to rats have caused mutagenesis and a bloom of cyanobacteria has been associated with a high human birth defect rate (Bourke & Hawes, 1983).

0.3 MEDICAL SURVEILLANCE/LABORATORY

A) Monitor liver enzymes. Monitor fluid and electrolyte balance in cases of severe or prolonged vomiting and diarrhea.

0.4 TREATMENT OVERVIEW

0.4.2 ORAL EXPOSURE

A) Gastric decontamination is not likely to be of use. Many of the toxins appear to be quickly absorbed and spread throughout the water ingested. Only if large volumes of contaminated water could be removed quickly might decontamination be of help.

B) No information was found regarding the use of charcoal. Charcoal administration may be considered at the physician's discretion.

1) ACTIVATED CHARCOAL: Administer charcoal as a slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.

C) These toxins produce diarrhea. Cathartics should not be given.

D) Although not seen in humans, respiratory failure is a primary cause of death in animals. Support respiratory function.

E) Monitor fluid and electrolyte balance. Prolonged periods of vomiting and diarrhea may result in loss of fluids and essential electrolytes.

F) Monitor liver enzymes. Although changes in liver enzymes have been reported in humans, the extent and result of the changes have yet to be determined. Liver failure has NOT been reported in humans.

G) Provide general supportive treatment as would be used for dysentery or enteritis.

0.4.4 EYE EXPOSURE

A) DECONTAMINATION: Irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

0.4.5 DERMAL EXPOSURE

A) OVERVIEW

1) DECONTAMINATION: Remove contaminated clothing and wash exposed area thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

0.5 RANGE OF TOXICITY

A) TOXIC DOSE - A toxic dose for humans has not been established. There are several toxic substances

involved with various toxic doses. The amount of each toxin may vary from day to day during any particular bloom.

B) ANIMAL DATA - Animal minimum lethal doses range from 10 to 40 mg/kg.

1.0 SUBSTANCES INCLUDED/SYNONYMS

1.1 THERAPEUTIC/TOXIC CLASS

A) There are over 50 genera of freshwater blue-green algae. One or more species may be present during an algae "bloom". This "bloom" may range from harmless to deadly (Spoerke & Rumack, 1985).

B) There are several types of toxins involved, they are released when the algae cell dies.

C) The following are synonyms for gastrointestinal illness caused by blue-green algae: Barcoo Fever, Barcoo Sickness, Barcoo Spews.

1.2 SPECIFIC SUBSTANCES

A) CONSTITUENTS OF THE GROUP

1. Anabaena flos-aquae
2. Anabaena lemmermannii
3. Anabaena torulosa
4. Aphanizomenon flos-aquae
5. Caelosphaerium keutzingianum
6. Cylindrospermosis raciborskii
7. Gloerichia echinulata
8. Lyngbya birgei
9. Lyngbya majuscula
10. Microcystis aeruginosa
11. Microcystis flos-aquae
12. Microcystis incerta
13. Nolularia spumigena
14. Nostoc rivulare
15. Oscillatoria species
16. Schizothrix calciola
17. References: Dillenberg & Dehnal, 1959; Yu et al, 1990

SYNONYMS FOR THE GROUP

1. Blue-green Algae
2. Cyanobacteria
3. Cyanophytes
4. Anatoxin A
5. 2-acetyl-9-azabicyclo(4.2.1)non-2,3-ene

1.4 DESCRIPTION

A) Cyanobacteria (blue-green algae) are phototropic "bacteria" which differ from other algae because they have no nuclear membrane. They grow in slow moving or stagnant water.

B) Although there are 50 or so genera of freshwater blue-green algae, the species most often related to poisoning are: Anabaena, Aphanizomenon, Microcystis, Schizothrix calcicola, Nolularia, Gloeotrichia,

and Achyta (Dillenberg & Dehnel, 1960).

C) The toxins of these algae are usually inside the cyanobacteria and are released only after the cell dies and/or disintegrates (Bourke & Hawes, 1983).

1) Use of algicides in public water supplies causes lysis of blue-green algae and the release of intracellular toxins, thus transiently increasing the concentration of dissolved toxins and potentially increasing human exposure if the reservoir is still in use. Degradation of the toxins can require several weeks (Steffensen et al, 1999).

D) "Annie, Fannie, and Mike" - common slang terms for TOXICOSIS involving Anabaena flos-aquae, Aphanizomenon flos-aquae, and Microcystis aeruginosa (Kerr et al, 1987).

E) TOXIC BLOOMS

1) Toxicity usually occurs during a "bloom." This is a period of rapid growth of various algae. The water may look "painted green" or have "scum" over its surface.
2) Poisonings occur during warm, dry weather that limits other drinking water and promotes rapid algae growth. Often a mild wind will blow consistently from one direction concentrating the algae against one shore.
3) The algae populations seen in a particular "bloom" may change rapidly, so samples need to be taken as soon as possible after a "bloom" is discovered. Not all blooms are toxic, and the type of toxins found may vary during any particular bloom (Mahmood et al, 1988).
4) Both toxic and non-toxic species may be found in the same bloom.
5)

TOXIN	PRODUCED BY
NEUROTOXINS	
Anatoxin-a	Anabaena, Aphanizomenon,
Homo-Anatoxin-a	Oscillatoria (Planktorthrix)
Anatoxin-a(s)	Anabaena, Oscillatoria (Planktorthrix)
LIVER TOXINS	
Cylindrospermopsin	Aphanizomenon, Cylindrospermopsis, Umezakia
Microcystins	Anabaena, Aphanocapsa, Hapalosiphon, Microcystis, Nostoc, Oscillatoria (Planktothrix)
Nodularins	Nodularia (brackis h water)
CONTACT IRRITANT/ DERMAL TOXINS	
Debromoaplysiatoxin,	
Lyngbyatoxin	Lyngbya (marine)
Aplysiatoxin	Schizothrix (marine)

Ref: Carmichael, 2001.

3.0 CLINICAL EFFECTS

3.1 SUMMARY OF EXPOSURE

3.1.1 ACUTE EXPOSURE

A) HUMANS - Ingestion of concentrations high enough to cause serious toxicity is uncommon. Gastrointestinal effects following ingestion and dermatitis following contact are the most common effects.

1) Pneumonia (uncommon), sore throat, fever, vomiting, diarrhea, lassitude, rhinitis, conjunctivitis, perioral blisters, dermatitis, mild liver enzyme elevations, and electrolyte imbalance have been reported.
2) GASTROINTESTINAL EFFECTS may include the following:
a) ONSET - 3 to 5 hours (abdominal cramping, diarrhea, nausea, vomiting)
b) SEVERITY - generally mild; can be severe
c) DURATION - usually 1 to 2 days
d) Adverse effects have resulted from immersion in or consumption of contaminated water, ingestion of fish from contaminated water, and recreation on waters which have cyanobacteria. The tastes and odors of contaminated water generally limit the amounts ingested.
3) Fatal hepatic failure was reported following the use of contaminated water in a hemodialysis unit in Brazil.

B) ANIMALS - The toxins are potent neuromuscular blocking agents in animals.
1) A characteristic animal death caused by one kind of blue-green algae (Aphanizomenon) includes irregular respirations, spastic twitching, loss of coordination, violent tremors, gaping mouth, and death by respiratory failure. The onset depends on species. Death may be rapid (animals die before they leave the water) or delayed 6 to 24 hours.
2) Animals do not like to drink the contaminated water, but will if sufficiently thirsty.

C) The effects seem to be much more serious in animals than in humans. It is not known if this is due to lower ingested doses in humans or differences in the reaction of animals to the toxin as compared to humans.

3.3 VITAL SIGNS

3.3.2 TEMPERATURE

A) FEVER - Pyrogenic reactions have been reported in patients on hemodialysis using water contaminated with lipopolysaccharides, possibly from cyanobacteria in the local water supply (Hindman et al, 1975). Testing of the public water supply for total microbes and cyanobacterial speciation were not performed; gram negative microbes may also have been a source of endotoxin.
1) Fever has occurred following ingestion of contaminated water (Dillenberg & Dehnel, 1960) (Hayman, 1992).

B) HYPOTHERMIA - Subnormal temperatures were reported in poisoned animals (Deem & Thorp, 1939).

3.4 HEENT

3.4.2 EYES

A) CONJUNCTIVITIS - Contact conjunctivitis has occurred in humans (Bourke & Hawes, 1983)(El Saadi & Cameron, 1993).

B) VISUAL DISTURBANCE - In a series of 131 patients with dialysis dependent renal failure who received hemodialysis with water contaminated with cyanotoxins (microcystins and cylindrospermopsin) 116 (89%) developed visual disturbances (Carmichael et al, 2001).

3.4.3 EARS

A) EARACHE, contact conjunctivitis, and swollen lips occurred in humans after swimming in a lake contaminated with Anabaena species (Bourke & Hawes, 1983).

3.4.4 NOSE

A) RHINITIS can occur (Elder et al, 1993).

3.4.5 THROAT

A) SORE THROAT resulted in humans who swallowed cyanobacteria-contaminated water during canoeing exercises (Turner et al, 1990).

3.5 CARDIOVASCULAR

3.5.3 ANIMAL STUDIES

A) ANIMAL STUDIES
1) HEMORRHAGE
a) Petechial hemorrhages of the heart are a consistent autopsy finding in animals (Senior, 1960).

3.6 RESPIRATORY

3.6.1 ACUTE EFFECTS

A) PNEUMONIA
1) Atypical pneumonia has been reported (Elder et al, 1993).
2) CASE SERIES - Pneumonia developed in 2 individuals 4 to 5 days after canoeing exercises in a reservoir contaminated with cyanobacteria (Turner et al, 1990). Ingestion of the water was suspected.

B) BRONCHOSPASM
1) A hay-fever-like syndrome was reported by Bourke and Hawes (1983).

3.6.3 ANIMAL STUDIES

A) ANIMAL STUDIES
1) PARALYSIS
a) Anatoxin-a (very fast death factor found in Anabaena) is an alkaloid which causes pre- and post-synaptic neuromuscular blockage which is not reversed by edrophonium or neostigmine.
b) It causes respiratory paralysis in mammals and seizures in fowl (Beasley et al, 1983) (Mahmood et al, 1988).
2) THROMBOSIS PULMONARY
a) The pentapeptide found in M. aeruginosa caused pulmonary thrombosis in injected mice (Slatkin et al, 1983).

3.7 NEUROLOGIC

3.7.1 ACUTE EFFECTS

A) HEADACHE

1) Headache has been reported following ingestion (Dillenberg & Dehnel, 1960)(Hayman, 1992) and canoeing exercises which may have resulted in ingestion of contaminated water (Turner et al, 1990).

B) MALAISE

1) Malaise can occur (Hayman, 1992).

3.7.3 ANIMAL STUDIES

A) ANIMAL STUDIES

1) PARALYSIS

a) Partial paralysis occurs in both animals and birds (Deem & Thorp, 1935). Aphanizomenon species contain a potent nerve and muscle blocking agent (Sawyer et al, 1968). Anatoxin-A (very fast death factor found in Anabaena) is an alkaloid which causes pre and postsynaptic neuromuscular blockage which is not reversed by edrophonium or neostigmine.

b) Respiratory paralysis has been reported in mammals and seizures in fowl (Beasley et al, 1983)(Mahmood et al, 1988).

3.8 GASTROINTESTINAL

3.8.1 ACUTE EFFECTS

A) GASTROENTERITIS

1) Nausea, vomiting and diarrhea occur in humans (Bourke & Hawes, 1983)(Spoerke & Rumack, 1985)(Turner et al, 1990)(Elder et al, 1993)(El Saadi et al, 1995).

2) Cases may appear as amebic dysentery. Onset is 3 to 5 hours, with recovery in 1 to 2 days (Dillenberg & Dehnel, 1960)(Libby & Erb, 1976).

3) These organisms or cyanobacteria-like bodies have been found in the stools of affected persons (Suave et al, 1986; (Hart et al, 1990)(Long et al, 1990).

4) In a series of 131 patients with dialysis dependent renal failure who received hemodialysis with water contaminated with cyanotoxins (microcystins and cylindrospermopsin) 116 (89%) developed nausea and vomiting (Carmichael et al, 2001).

B) ABDOMINAL PAIN

1) Abdominal pain has been reported (Turner et al, 1990).

C) BLISTER

1) Blistering around the mouth has occurred in humans exposed to algal bloom of Microcystis aeruginosa (Turner et al, 1990)(Edney, 1990) and contact with water contaminated with Anabaena circinalis and other cyanobacteria (El Saadi & Cameron, 1993)(El Saadi et al, 1995).

D) LOSS OF APPETITE

1) Anorexia may occur (Hayman, 1992).

3.9 HEPATIC

3.9.1 ACUTE EFFECTS

A) LIVER ENZYMES ABNORMAL

1) Elevated liver enzymes (gamma-glutamyl-transpeptidase and alanine aminotransferase) have

been documented in residents who drank from a contaminated reservoir. Enzyme levels were normal before and after the cyanobacteria's bloom period (Falconer et al, 1983)(Hawkins et al, 1985).

B) HEPATOMEGALY

1) Tender hepatomegaly was present after Cylindrospermopsis raciborskii ingestion (Hayman, 1993).

C) HEPATIC FAILURE

1) At a Brazil dialysis center in 1996, 131 patients developed abdominal pain, nausea, vomiting dizziness, lethargy, myalgia, and in severe cases, visual disturbances and grand mal seizures, associated with hemodialysis. One hundred patients developed liver failure. One month later, 25 patients had died. Within 7 months, approximately 60 patients had died either from direct hepatotoxic effects or indirectly from complications, such as sepsis, gastrointestinal bleeding, and cardiovascular disturbances.

a) It was determined, by enzyme-linked immunoabsorbent assay, that the water used at the dialysis center came from a reservoir contaminated with microcystins and cylindrospermiopsin produced by cyanobacteria. Serum and liver samples taken before and after death confirmed the presence of microcystins (Carmichael et al, 2001)(Jochimsen et al, 1998)(Pouria et al, 1998).

3.9.3 ANIMAL STUDIES

A) ANIMAL STUDIES

1) HEPATOCELLULAR DAMAGE

a) Elevated liver enzymes have been documented in animals that drank from a contaminated reservoir. These elevated enzymes were not associated with illness (Falconer et al, 1983).

b) Hepatoenteritis and toxic liver injury is common with M. aeruginosa (Bourke & Hawes, 1983)(Jackson et al, 1984)(Galey et al, 1987). A distinct hemorrhagic necrosis of the liver has occurred in animals (Carmichael et al, 1985) Yu et al, 1990).

c) Lesions shown by electron microscope were aggregation of endoplasmic reticulum with displacement of subcellular organelles, toward the edges of the hepatocyte and vacuolation of the contents of severely affected cells (Jackson et al, 1984).

3.10 GENITOURINARY

3.10.1 ACUTE EFFECTS

A) ALBUMINURIA

1) Patients with "Palm Island Mystery Disease", believed to be from drinking water contaminated with Cyclindrospermopsis raciborskii, developed glycosuria, proteinuria, ketonuria, and occasionally hematuria (Byth, 1980)(Hayman, 1992). Copper poisoning may have contributed to these effects (Prociv, 1987).

3.12 FLUID-ELECTROLYTE

3.12.1 ACUTE EFFECTS

A) DEHYDRATION

1) Fluid and electrolyte loss may occur if the gastroenteritis is severe or prolonged (Byth, 1980).

3.13 HEMATOLOGIC

3.13.3 ANIMAL STUDIES

A) ANIMAL STUDIES
1) THROMBOCYTOPENIA
a) The pentapeptide found in M. aeroginosa caused thrombocytopenia and pulmonary thrombi when injected into mice (Slatkin et al, 1983).

3.14 DERMATOLOGIC

3.14.1 ACUTE EFFECTS

A) DERMATITIS
1) CASE REPORT - A human developed allergic erythematous papulovesicular dermatitis after swimming in contaminated water (Bourke & Hawes, 1983).
2) Rashes, itching and/or perioral blistering have been reported in persons who had contact with water which had confirmed or suspected cyanobacteria contamination (Soong et al, 1992)(El Saadi & Cameron, 1993)(El Saadi et al, 1995).

3.15 MUSCULOSKELETAL

3.15.1 ACUTE EFFECTS

A) MUSCLE WEAKNESS
1) Humans have reported muscle weakness and pain (Dillenberg & Dehnel, 1960).

B) JOINT PAIN
1) Pain in the limbs and joints have occurred in exposed humans (Dillenberg & Dehnel, 1960).

3.15.3 ANIMAL STUDIES

A) ANIMAL STUDIES
1) PARALYSIS
a) Animals have developed progressive muscle weakness, progressing to paralysis (McLeod & Bondar, 1952).

3.17 METABOLISM

3.17.3 ANIMAL STUDIES

A) ANIMAL STUDIES
1) CHOLINESTERASE DECREASED
a) Anticholinesterase activity has occurred in animals after ingestion of anatoxin-a(s) from Anabaena flos-aquae. Effects included salivation, lacrimation, urinary incontinence and defecation. Nicotinic effects were fasciculations, seizures and respiratory paralysis (Mahmood et al, 1988).

3.19 IMMUNOLOGIC

3.19.3 ANIMAL STUDIES

A) ANIMAL STUDIES
1) IMMUNE SYSTEM DISORDER
a) Intraperitoneal injection of cyanobacteria cells caused suppression of the number of plaque-forming cells in mice at high doses (0.4 mg/mouse) and lower concentrations (0.2 mg/mouse) caused immunostimulation (Mundt et al, 1991).
2) IN-VITRO STUDIES
a) Cyanobacterial extracts inhibited (3)H-thymidine incorporation into mitogen-stimulated human lymphocytes (Mundt et al, 1991).

3.21 CARCINOGENICITY

3.21.4 HUMAN STUDIES

A) CARCINOMA
1) Exposure to cyanobacteria in drinking water has been associated with an increased risk of hepatocellular carcinoma in a study conducted in China (Falconer, 1999).

3.21.5 ANIMAL STUDIES

A) CARCINOMA
1) MICROCYSTINS are known to be potent tumor promoters when tested in animals (Nishiwaki-Matsushima et al, 1992).

3.22 GENOTOXICITY

3.22.1 SUMMARY

A) M. aeruginosa extracts fed to rats have caused mutagenesis and a bloom of cyanobacteria has been associated with a high human birth defect rate (Bourke & Hawes, 1983).

4.0 MEDICAL SURVEILLANCE/LABORATORY

4.1 MONITORING PARAMETERS/LEVELS

4.1.1 SUMMARY

A) Monitor liver enzymes. Monitor fluid and electrolyte balance in cases of severe or prolonged vomiting and diarrhea.

4.1.2 SERUM/BLOOD

A) BLOOD/SERUM CHEMISTRY
1) Serum levels are not useful except for identification. No serological test for exposure exists, but one is being worked on by Chester Public Health Laboratory of the UK (Elder et al, 1993).
2) Monitor liver enzymes should be monitored. Monitor fluid and electrolytes if vomiting and/or diarrhea are severe or prolonged.

4.1.3 URINE

A) URINALYSIS

1) Obtain urinalysis for detection of protein, glucose, ketone, and blood.

4.1.5 OTHER

A) OTHER

1) OTHER

a) To aid in diagnosis, feces and stomach contents may be examined for the presence of cyanobacterial cells (Elder et al, 1993).

4.3 METHODS

A) MULTIPLE ANALYTICAL METHODS

1) Methods of identifying cyanobacteria from stool and vomitus (Elder et al, 1993), and for differentiating cyanobacteria-like bodies from cyanobacteria, are available (Long et al, 1991) (McIntyre & Lyons, 1992)(Gascon et al, 1993).

2) The toxic heptapeptides from Microcystis aeruginosa can be identified and purified by HPLC (Runnegar et al, 1986). ODS-silica gel cartridge and high performance liquid chromatography with ODS-gel is an effective method (Watanabe et al, 1988)(Krishnamurthy et al, 1986).

3) Anatoxin A is frequently degraded quickly in toxic blooms and is difficult to find. Smith and Lewis (1987) detailed a method of isolating dihydro-anatoxin A, which is a metabolite.

4) A variety of methods are available for the detection of microcystin in water (Lam et al, 2000).

a) The mouse bioassay is easy to interpret and technically simple but expensive and labor intensive.

b) HPLC allows for accurate detection and quantification of different toxins, but has relatively low sensitivity and often requires preconcentration and pretreatment.

c) ELISA methods can detect different structural variants of toxins (however, a wide spectrum of antibodies may be required) and commercial kits are available for semiquantitative detection.

d) Cytotoxicity assays are highly sensitive if primary liver cells are used (but their production is labor intensive); there are established cell lines that provide for routine testing, but they are generally less sensitive.

e) A radiometric protein phosphate inhibition assay is specific for inhibitors of serine/threonine protein phophatases type 1 and 2A and is highly sensitive, but it is not specific for various structural variants, and requires freshly prepared radiolabelled substrate and subsequently the disposal of radioactive waste.

f) A colorimetric protein phosphate inhibition assay is rapid and simple, highly sensitive and has high throughput, but is not specific for various structural variants of microcystins and requires a pure preparation of serine/threonine protein phosphatases type 1 or 2A.

5) Bioassays for cyanobacterial toxins have been developed using a protozoan (Spirostomum ambiguum), crustaceans (Thamnocephalus platurus) and cladoceran (Daphnia magna) (Tarczynska et al, 2001).

6.0 TREATMENT

6.1 LIFE SUPPORT

A) Support respiratory and cardiovascular function.

6.4 MONITORING

A) Monitor liver enzymes. Monitor fluid and electrolyte balance in cases of severe or prolonged vomiting and diarrhea.

6.6 DERMAL EXPOSURE

6.6.1 DECONTAMINATION

A) DERMAL DECONTAMINATION

1) Remove contaminated clothing and wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists after washing.

6.7 EYE EXPOSURE

6.7.1 DECONTAMINATION

A) Remove contact lenses and irrigate exposed eyes with copious amounts of room temperature 0.9% saline or water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist after 15 minutes of irrigation, an ophthalmologic examination should be performed.

6.8 ORAL/PARENTERAL EXPOSURE

6.8.1 PREVENTION OF ABSORPTION/PREHOSPITAL

A) EMESIS -

1) Emesis is not likely to be useful. Many of the toxins appear to be quickly absorbed and spread throughout the water ingested.

B) ACTIVATED CHARCOAL -

1) No information was found regarding the use of charcoal in cyanobacteria ingestions. Charcoal use is at the physician's discretion.

6.8.2 PREVENTION OF ABSORPTION

A) ACTIVATED CHARCOAL

1) No information was found regarding the use of charcoal in cyanobacteria ingestions (Cooney, 1995). Charcoal use is at the physician's discretion.

2) CHARCOAL ADMINISTRATION

a) Consider administration of activated charcoal after a potentially toxic ingestion (Chyka & Seger, 1997). Administer charcoal as an aqueous slurry; most effective when administered within one hour of ingestion.

3) CHARCOAL DOSE

a) Use a minimum of 240 milliliters of water per 30 grams charcoal (FDA, 1985). Optimum dose not established; usual dose is 25 to 100 grams in adults and adolescents; 25 to 50 grams in children aged 1 to 12 years (or 0.5 to 1 gram/kilogram body weight) ; and 1 gram/kilogram in infants up to 1 year old (USP DI, 2002)(Chyka & Seger, 1997).

1) Routine use of a cathartic with activated charcoal is NOT recommended as there is no evidence that cathartics reduce drug absorption and cathartics are known to cause adverse effects such as nausea, vomiting, abdominal cramps, electrolyte imbalances and occasionally hypotension (Barceloux et al, 1997).

b) ADVERSE EFFECTS/CONTRAINDICATIONS

1) Complications: emesis, aspiration (Chyka & Seger, 1997). Aspiration may be

complicated by acute respiratory failure, ARDS or bronchiolitis obliterans (Pollack et al, 1981; Harris & Filandrinos, 1993; (Elliot et al, 1989) Harsh, 1986; (Rau et al, 1988) (Golej et al, 2001)(Graff et al, 2002). Refer to the ACTIVATED CHARCOAL/TREATMENT management for further information.
2) Contraindications: unprotected airway, gastrointestinal tract not anatomically intact, therapy may increase the risk or severity of aspiration; ingestion of most hydrocarbons (Chyka & Seger, 1997).

6.8.3 TREATMENT

A) AIRWAY MANAGEMENT

1) Although not reported in humans, respiratory failure is a primary cause of death in animals. Support respiratory function. Anticholinergics and oximes have not been tried in cases of Anatoxin-a poisoning.

B) FLUID/ELECTROLYTE BALANCE REGULATION

1) Monitor fluid and electrolytes and treat with intravenous or oral hydration as indicated. Prolonged periods of vomiting and/or diarrhea may result in loss of fluids and essential electrolytes.

C) MONITORING OF PATIENT

1) Monitor liver enzymes. Although changes in liver enzymes have been reported in humans, the extent and result of these changes have yet to be determined. Liver failure has NOT been seen in humans. Treatment is supportive.

D) GENERAL TREATMENT

1) Treatment in humans has been as for dysentery or enteritis. Animals are most often dead when found or recover uneventfully without treatment. Antibiotics and respiratory stimulants have been used, but there is little evidence that they changed outcome.

7.0 RANGE OF TOXICITY

7.1 SUMMARY

A) TOXIC DOSE - A toxic dose for humans has not been established. There are several toxic substances involved with various toxic doses. The amount of each toxin may vary from day to day during any particular bloom.

B) ANIMAL DATA - Animal minimum lethal doses range from 10 to 40 mg/kg.

7.4 MAXIMUM TOLERATED EXPOSURE

A) GENERAL/SUMMARY

1) TOXIC DOSE - A toxic dose for humans has not been established; there are several toxic substances involved, with various toxic doses. The amount of each toxin may vary from day to day during any particular bloom.

7.6 TOXICITY INFORMATION

7.6.1 TOXICITY VALUES

A) Microcystis aeruginosa
1) LD50 - (INTRAPERITONEAL) MOUSE:
a) 100 mg/kg -- Freeze dried cells (He et al, 1990)
b) 1 mg/kg -- Purified toxin (He et al, 1990)
c) 100-300 mg/kg -- Various blooms (He et al, 1990)

7.8 OTHER

A) OTHER
1) CONCENTRATION LEVEL
a) LIVER - The concentration of microcystins found in the liver tissue of 17 hemodialysis patients, who died due to acute liver failure caused by contaminated water, ranged from 0.03 to 0.60 grams per kilogram (median, 0.18 grams/kilogram) (Jochimsen et al, 1998).

8.0 KINETICS

8.1 ABSORPTION

A) SUMMARY
1) Absorption: Not well studied but since death can occur rapidly in animals (Spoerke & Rumack, 1985)(Smith & Lewis, 1987), absorption is thought to be rapid.

8.2 DISTRIBUTION

8.2.1 DISTRIBUTION SITES

A) TISSUE/FLUID SITES
1) When radiolabled iodinated toxic heptapeptides were administered to mice, the greatest concentrations were found in the liver. Kidneys showed low but measurable radioactivity up to 24 hours post injection (Runnegar et al, 1986).

8.3 METABOLISM

8.3.2 METABOLITES

A) GENERAL
1) Anatoxin A (2-acetyl-9-azabicyclo(4.2.1)non-2,3-ene) is bioreduced to both a "chair" and "boat" form of dihydro Anatoxin A, 2-acetyl-9-azabicyclo(4.2.1)nonane (Smith & Lewis, 1987).

9.0 PHARMACOLOGY/TOXICOLOGY

9.2 TOXICOLOGIC MECHANISM

A) TOXINS - SITE OF ACTION -
1) There are two main types of toxins in these cyanobacteria. The first are neurotoxic alkaloids (anatoxins) and the second are hepatotoxic peptides also called fast-death factor, microcystine, cyanoginosin, cyanoviridin, and cyanogenosin (Anon, 1988)(Kungsuwan et al, 1988).
2) Lipopolysaccharides (endotoxins) are also present and are believed to cause the skin rashes, dermal and eye irritation following contact with cyanobacteria-contaminated water (Baxter, 1991).

B) TOXIN TYPES - Toxins included in these algae include alkaloids, polypeptides, pteridines and lipopolysaccharides (endotoxins).

C) TOXINS - COMPOSITION -

1) Botes et al (1982a-b; 1984) found four different toxins in M. aeruginosa, all thought to be pentapeptide. Each contained three common pairs and a unique pair of amino acids. The pairs were combinations of leucine and arginine, tyrosine and arginine, leucine and alanine, or tyrosine and alanine (Botes et al, 1982b).

2) The hepatotoxin in M. aeruginosa is a pentapeptide or a double pentapeptide (Bourke & Hawes, 1983).

D) TOXINS - SPECIFIC -

1) ANATOXIN-A (ANTX-A) is manufactured by Anabaena flos-aquae. It is a potent depolarizing neuromuscular blocking agent active at both the nicotinic and muscarinic receptors (Mahmood & Carmichael, 1986)(Mahmood et al, 1988).

2) ANATOXIN-A(S), also from Anabaena flos-aquae has a different mechanism of action, producing intense salivation.

a) It is thought to be a peripheral-acting organophosphorus anticholinesterase agent (Mahmood & Carmichael, 1986). A. flos-aquae is also known to contain hepatotoxic peptides (Krishnamurthy et al, 1986).

b) In animals, anatoxin-(s) most frequently is seen with pigs, dogs, and waterfowl. Ruminants are more resistant (Beasley, 1990).

c) Anatoxin-a(s) inhibits cholinesterases in blood, lung, and muscle. Retinal and brain cholinesterases are not affected (Beasley, 1990).

3) APHANTOXIN - The toxin found in Aphanizomenon flos-aquae is very similar to both saxitoxin (paralytic shellfish poisoning) and tetrodotoxin (Adelman et al, 1982)(Jackim & Gentile, 1968).

a) Data obtained from axon testing of the giant squid demonstrated that aphantoxin is a potent and specific inhibitor of the voltage-dependant sodium ion channel (Adelman et al, 1982).

4) MICROCYSTIN - is a hepatotoxic algaltoxin. Experiments have shown that cell injury was not due to extracellular but due to intracellular calcium flux (Bunner & Morris, 1990).

a) Microcystis toxins are called microcystins and undergo different rates of decomposition. In one in vitro experiment microcystin YR was found to decompose faster than microcystin LR (Watanabe et al, 1992).

b) Microcystin LR (a cyclic heptapeptide) is a hepatotoxin. When tested in rodents, the lowest consistent lethal dose was 160 mcg/kg in rats and 100 mcg/kg in mice (Hooser et al, 1989).

1) Hepatic lesions have been seen as soon as 10 minutes after inspection of rats injected with microcystin LR. Centrilobular necrotic cells were noted within 60 minutes (Hooser et al, 1990).

c) Microcystins bind and inhibit protein phosphatase 1 and 2A in the hepatocyte, disrupting maintenance of cell structure and function (Gilroy et al, 2000).

11.0 PHYSICOCHEMICAL

11.1 PHYSICAL PARAMETERS

11.1.1 PHYSICAL CHARACTERISTICS

A) The Microcystis aeruginosa liver toxin is non-volatile, relatively heat stable.

11.1.2 MOLECULAR WEIGHT

A) Not applicable

11.2 CHEMICAL PARAMETERS

11.2.3 SOLUBILITY

A) IN WATER
1) soluble in water

B) IN ORGANIC SOLVENTS
1) soluble in alcohol and acetone

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